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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,742	07/20/2001	Kazuhito Miyauchi	2603.2	9051

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EXAMINER

SAUCIER, SANDRA E

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 05/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/889,742

Applicant(s)

Miyachi et al.

Examiner

Sandra Saucier

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Mar 11, 2003
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above, claim(s) 19-25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on Jul 20, 2001 is/are a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 1, 4 6) ☐ Other:

Art Unit: 1651

DETAILED ACTION

Claims 1-25 are pending. Claims 1-18 are considered on the merits. Claims 19-25 are withdrawn from consideration as being drawn to a non-elected invention.

Election/Restriction

Claims 19-25 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention. Election was made without traverse in Paper No. 6.

Information Disclosure Statement

The listing of the references on PTO 1449 is incomplete. A proper citation includes AUTHOR, TITLE, journal, volume, number, inclusive pages, (month), year. The citations are missing the author and title of the articles.

MPEP37 CFR 1.98(b) requires that each U.S. patent listed in an information disclosure statement be identified by patentee, patent number, and issue date. Each foreign patent or published foreign patent application must be identified by the country or patent office which issued the patent or published the application, an appropriate document number, and the publication date indicated on the patent or published application. Each publication must be identified by author (if any), title, relevant pages of the publication, date and place of publication. The date of publication supplied must include at least the month and year of publication, except that the year of publication (without the month) will be accepted if the applicant points out in the information disclosure statement that the year of publication is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the particular month of publication is not in issue. The place of publication refers to the name of the journal, magazine, or other publication in which the information being submitted was published.

The improper citations have been lined through on the PTO 1449. Please submit another, corrected PTO 1449.

The first page (276) from the article from the Journal of Clinical and Experimental Medicine 172 (5) :276-280 is not complete. The page has been improperly photocopied and is not readable because half the page has been truncated. Please resubmit a complete copy of this article, if it is wished to

Art Unit: 1651

have it considered.

Claim Rejections - 35 USC § 112

INDEFINITE

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is confusing because it uses the term "free glycerol" twice to designate both glycerol which was present in the initial sample and the glycerol generated from the triglycerides in the original sample. Please see the explanation and interpretation of the claim below in the anticipatory rejection.

Claim 1 is confusing because it states that it is a method for quantitating triglyceride in a particular lipoprotein, but fails to have any steps which select a particular lipoprotein in the sample. The claim appears to be incomplete in this regard.

Claim 3 is confusing because it uses "the generated hydrogen peroxide" and refers to claim 2 where the generated hydrogen peroxide is said to be eliminated, not quantitated. The quantitation is associated with the second generation of hydrogen peroxide after treatment with lipoprotein lipase, not the first generation of hydrogen peroxide which is associated with the elimination of free glycerol.

Claim 7 has no antecedent basis for the recitation of "the surfactant and/or enzyme".

Claim 11 has no antecedent basis for "and/or enzyme that allows the reaction" etc..

Claim 12 recites "'allowing the reaction of lipoproteins other than the particular one used in elimination of hydrogen peroxide" is not interpretable. The particular lipoprotein is not used in the elimination of hydrogen peroxide.

The claims are also confusing because while claim 1 recites that it is a method for quantitation triglyceride in A PARTICULAR LIPOPROTEIN, the sample DOES NOT REQUIRE THE PRESENCE OF A MIXTURE OF LIPOPROTEINS and may,

Art Unit: 1651

therefore consist of only one type of lipoprotein such as HDL.

The claims are replete with abbreviations and parenthetical inclusions. Please do not use abbreviations or parenthesis in the claims as it cannot be determined if the parenthetical inclusions are meant to further limit or expand the claim and abbreviations may permit unfavorable interpretations.

Please carefully redraft the claims in order to clearly delineate the steps of the method. Many of the claims are so unclear that they cannot be properly evaluated for prior art purposes. In the interest of compact prosecution, the examiner has interpreted them as far as possible and applied art.

It is suggested that the claim steps be labeled step a) which would be the elimination of free glycerol, and step b) which would be the quantitation of triglyceride by hydrolysis of the triglyceride and generation of the color reaction, and that the dependent claims refer to these steps in order to clarify the claimed process.

Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action: A person shall be entitled to a patent unless (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent, (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by JP 57-137858 [IDS].

The claims are directed to a method for quantitating triglycerides in a particular lipoprotein comprising:

eliminating the free glycerol from a sample containing free glycerol and triglyceride in the particular lipoprotein,

allowing the resultant sample to react with lipoprotein lipase to produce glycerol from the triglyceride and a system which generates H_2O_2 from the produced glycerol and quantitating the H_2O_2 .

Art Unit: 1651

The references are relied upon as explained below.

JP 57-137858 discloses a method of quantitating triglyceride in a sample comprising: eliminating the free glycerol from the sample using periodic acid, allowing the resultant sample to react with lipoprotein lipase to produce glycerol from the triglyceride and generating H_2O_2 from the glycerol and reacting it with a chromogen (4-aminoantipyrine/p-chlorophenol, Trinder's chromogen) to quantitate the amount of triglyceride originally present in the sample.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by JP 59-011197 [IDS] or Yoshida *et al.* [U].

The claims were discussed above.

JP 59-011197 discloses a method of quantitating triglycerides in a sample comprising:
eliminating the free glycerol by reacting it with glycerol kinase, glycerophosphate oxidase, peroxidase and a phenol derivative, then reacting the resultant sample with lipoprotein lipase and aminoantipyrine/anisidine and the developed color is measured to quantitate triglycerides.

Yoshida *et al.* disclose a method for the determination of triglyceride concentration in a sample with free glycerol comprising:

eliminating the free glycerol from the sample using glycerol kinase, glycerol 3-phosphate oxidase to generate H_2O_2 ,

allowing the resultant sample to react with lipoprotein lipase, glycerol oxidase and peroxidase and developing color with p-chlorophenol, 4-aminoantipyrine and measuring the color intensity which is correlated with triglyceride concentration in the sample.

Claims 1-5, 7-13, 15-18 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by JP 58-047499 [IDS].

The claims were discussed above.

Art Unit: 1651

JP 58-047499 discloses a method of quantitating triglycerides in serum comprising:
treating the serum with glycerol kinase, glycerol-3-phosphate oxidase, peroxidase, ATP, Triton X 100 in buffer to remove free glycerol and then lipoprotein lipase, 4-aminoantipyrine and Triton X 100 and measurement of the resultant color.

Please note that Triton X 100 is added both during the elimination of free glycerol and during the lipase addition in the reference and that Triton X 100 is one of the surfactants disclosed as being useful in the process of selecting a particular lipoprotein on page 15 of the specification. Although the reference is silent with respect to the effect of the detergent/surfactant, it is reasonable to expect that the same results would accrue from the addition of the same detergent/surfactant as stated in the specification to be added to the sample in the selection of a particular lipoprotein fraction.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action: (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-13, 15, 16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshida *et al.* [U] in view of US 4,215,993 [A] or EP 76211 [N].

The claims are directed to a method for quantitating triglycerides in a particular lipoprotein comprising:

eliminating the free glycerol from a sample containing free glycerol and

Art Unit: 1651

triglyceride in the particular lipoprotein,

allowing the resultant sample to react with lipoprotein lipase to produce glycerol from the triglyceride and a system which generates H_2O_2 from the produced glycerol and quantitating the H_2O_2 .

The references are relied upon as explained below.

Yoshida *et al.* disclose a method for the determination of triglyceride concentration in a sample with free glycerol comprising:

eliminating the free glycerol from the sample using glycerol kinase, glycerol 3-phosphate oxidase to generate H_2O_2 ,

allowing the resultant sample to react with lipoprotein lipase, glycerol oxidase and peroxidase and developing color with p-chlorophenol, 4-aminoantipyrine and measuring the color intensity which is correlated with triglyceride concentration in the sample.

The references lack the disclosure of the determination of triglyceride content from a specific lipoprotein fraction from a sample which contains a mixture of lipoproteins using detergents or polyanions/divalent metals.

US 4,215,993 discloses a method of separating various lipoprotein fractions from serum using polyanions in order to determine the concentration of lipoprotein components by desired methods (claims 17 and 23 and col. 1, l. 15).

EP 76211 discloses a method of separating various lipoprotein fractions from serum using polyanions/divalent cations or detergents in order to determine the individual fractions' components such as triglyceride (abstract).

The use of the methods described in US 4,215,993 or EP 76211 to isolate a particular lipoprotein fraction in order to quantitate the triglyceride concentration in that particular lipoprotein fraction by the method of Yoshida *et al.* would have been obvious at the time of invention to one of ordinary skill in the art because EP 76211 suggests the use of polyanions and/ or detergents for the determination of triglycerides in specific lipoprotein fractions (abstract).

Art Unit: 1651

Further, US 4,215,993 specifically states that the use of polyanions with serum to precipitate high density lipoproteins allows for determination of triglyceride by a desired method, which may be the determination disclosed by Yoshida *et al.*.

Claims 1-12, 14, 15, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ohkubo *et al.* [W] in view of US 4,215,993 [A] or EP 76211 [N].

The claims have been explained above.

Ohkubo *et al.* disclose a method for the determination of triglyceride concentration in a sample with free glycerol comprising:

eliminating the free glycerol from the sample using glycerol oxidase and peroxidase to generate H_2O_2 ,

allowing the resultant sample to react with lipoprotein lipase and peroxidase and developing color with 4-aminoantipyrine and EMAE and measuring the color intensity which is correlated with triglyceride concentration in the sample.

The reference lacks the use of polyanions/detergents to select a particular lipoprotein for the determination of triglyceride concentration.

US 4,215,993 or EP 76211 were discussed above.

The use of the methods described in US 4,215,993 or EP 76211 to isolate a particular lipoprotein fraction in order to quantitate the triglyceride concentration in that particular lipoprotein fraction by the method of Ohkubo *et al.* would have been obvious at the time of invention to one of ordinary skill in the art because EP 76211 suggests the use of polyanions and/ or detergents for the determination of triglycerides in specific lipoprotein fractions (abstract).

Further, US 4,215,993 specifically states that the use of polyanions with serum to precipitate high density lipoproteins for desired determinations and specifically mention is triglyceride determination which is the same kind of determination disclosed by Ohkubo *et al.*.

Art Unit: 1651

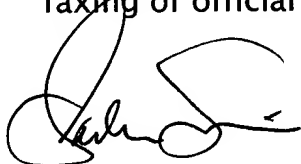
Whether one adds the detergent/polyanion reagents before, after or during the elimination of free glycerol from the sample is considered to be an element of experimental design which is well within the purview of one of ordinary skill in the art in the absence of evidence of criticality.

One of ordinary skill in the art would have been motivated at the time of invention to perform the claimed method in order to obtain the results as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

All elements of the claimed method are disclosed in the prior art.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1651. The supervisor for 1651 is M. Wityshyn, (703) 308-4743. The normal work schedule for Examiner Saucier is 8:30 AM to 5:00 PM Monday and Tuesday and 8:30 AM to noon on Wednesday.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (703) 308-1084. Status inquiries must be directed to the Customer Service Desk at (703) 308-0197 or (703)-308-0198. The number of the Fax Center for the faxing of official papers is (703) 872-9306 or for after finals (703) 872-9307.



Sandra Saucier
Primary Examiner
Art Unit 1651
May 7, 2003